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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,652	09/24/2001	Claudio De Simone	2818-58	5995

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,652	DE SIMONE, CLAUDIO	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *35-39 and 41-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *35-39 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/15/2004 has been entered.

Status of claims

Claims 35-39 and 41-43 as amended are pending and under examination {12/04/2003}.

Claims 1-34 and 40 are canceled by applicant.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Italy on 9 June 1999. It is noted, however, that applicant has not filed a certified copy of the RM99A000376 application as required by 35 U.S.C. 119(b).

With respect to International Application PCTIT00/00230 applicant has to provide proof of copendency. MPEP 1896.

Deposit

The deposit requirement for the strain *Lactobacillus brevis* CD2 accession No. DSM 11988 has been in the paper(s) filed 6/20/2003.

Claim Objections

Claims 38, 39 and 41-43 are objected to because of the following informalities:

Claim 38 appears to contain some typing error that is "and" in place of "wherein" before the phrase "additional bacteria" (see line 2).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Written disclosure

Claims 35-39 and 41-43 are rejected under 35 U.S.C. 112, *first paragraph*, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 35, with dependent claims 38, 39 and 41-43, is drawn to a method of using an alkaline sphingomyelinase derived from the bacterial strain DSM 11988 *Lactobacillus brevis*. The specification does not describe such enzyme. There is only one reference related to the claimed subject matter such as being "similar" (specification page 13, line 11) to the results obtained in the experiments with bacteria belonging to *Streptococcus thermophilus*.

Claims 38, 39 and 41-43, that depend on claim 35, recite the use of an additional alkaline sphingomyelinase of bacterial origin.

Thus, the following rejection is about the use of a genus of alkaline sphingomyelinase of bacterial origin.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). To fully describe a genus of material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Thus, for a product to be sufficiently described one needs to know structure, correlation between structure and function and combination of identifying characteristics.

In the instant specification the genus of an enzyme "alkaline sphingomyelinase of bacterial origin" is described as a crude preparation having unidentified contents and chemical structure in a form of a sonicated sample of lyophilized bacterial cells belonging to *Streptococcus thermophilus*. The sonicated bacterial sample is assayed for hydrolysis of sphingomyelin in the *in vitro* system. For example: see specification page 10, lines 7 and 25; page 11, lines 14-27 and page 12, lines 1-6. No other bacterial sample-derived "alkaline sphingomyelinase" are disclosed. With respect to the strain DSM 11,988, it is said to have "similar results" (specification page 13, line 11) without the definition of the term "similar".

Bacteria are known to contain various hydrolytic enzymes and enzymes are known to have various isoforms having the similar function but different structural, physical and immunological characteristics. In the instant case, the claimed enzyme or enzymatic preparation is a sonicated sample of bacterial cells that is not characterized by any specific contents and/or any chemical structure. The specification does not describe any correlation between function (hydrolysis of sphingomyelin) and structure of alkaline sphingomyelinase of bacterial origin. The specification does not describe any specific combination of identifying characteristics of the bacterial sonicated samples that would demonstrate function and/or structure associated with alkaline sphingomyelinase of bacterial origin. One the other hand, the prior art does not describe "alkaline sphingomyelinase of bacterial origin" and no specific compound of the alkaline sphingomyelinase has been isolated from bacteria. The Enzyme databases {NiceZyme or TrEMBL} indicate alkaline sphingomyelinase as a hypothetical protein isolated from rat intestine and human colon tissue only.

Thus, in the absence of disclosure about structure, correlation between function and structure and combination of identifying characteristics there is no sufficient support for the enzymatic compound "alkaline sphingomyelinase of bacterial origin" as claimed. Further, in the absence of disclosure about structure, correlation between function and structure and combination of identifying characteristics there is no sufficient support to provide a link for the alkaline sphingomyelinase related similarities between the claimed strain DSM 11,988 and the other bacteria or bacterial samples that have been assayed for hydrolysis of sphingomyelin as disclosed. Therefore, without disclosure of the claimed enzyme one cannot visualize what is similar as related to the use of strain DSM 11,988.

Since specification fails to define those features of alkaline sphingomyelinase of bacterial origins that are commonly possessed by bacterial samples and that distinguish them from each other and other members of the genus, one skilled in the art cannot visualize or recognize the identity of the members of the genus in order to use or to administer the claimed product for treatment of all asserted conditions as claimed. Moreover, the specification fails to describe examples of *in vivo* administration of alkaline sphingomyelinase of bacterial origins including alkaline sphingomyelinase derived from the claimed strain DSM 11,988.

Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention, the genus of alkaline sphingomyelinase of bacterial origins including alkaline sphingomyelinase derived from the strain DSM 11988.

Enablement

Claims 35-39 and 41-43 are rejected under 35 U.S.C. 112, *first paragraph,* as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 35, with all dependent claims, is drawn to a method of preventing or treating disorders of intestinal development, cancer, etc. by administering a prophylactic or therapeutic amount of alkaline sphingomyelinase derived from bacterial strain DSM 11988 *Lactobacillus*

brevis. Claims 38, 39 and 41-43, that depend on claim 35, recite the use of an additional alkaline sphingomyelinase of bacterial origin.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the scope of the claims that encompass a product such as an alkaline sphingomyelinase of bacterial origin including alkaline sphingomyelinase derived from the strain DSM 11988. Since the specification fails to define those features of alkaline sphingomyelinase of bacterial origin that are commonly possessed by bacterial samples and that distinguish them from each other and other members of the genus, one skilled in the art cannot visualize or recognize the identity of the members of the genus in order to provide prophylactic or therapeutic amount of the claimed product for treatment of all asserted conditions as claimed.

With regard to the prior art, the fact that the alkaline sphingomyelinase in found in the intestinal samples of animals including humans does not mean that the bacterial preparation with the alkaline sphingomyelinase activity would prevent or treat all asserted conditions as claimed because correlation between alkaline sphingomyelinase of bacterial origin and all and each claimed conditions is not established. The prior art finding that colorectal cancer or tumorigenesis is associated with a deficiency of the intestinal alkaline sphingomyelinase (Rui-Dong Duan, 1998; IDS filed 9/24/01, reference 5} does not necessarily mean that the bacterial

product with alkaline sphingomyelinase activity including the strain DSM 11988 derived product would prevent or treat colorectal cancer as well as other asserted conditions as presently claimed.

With regard to the amount of direction or guidance presented in the as-filed specification, the fact that bacterial strain DSM 11988 exhibits some similarities to *Streptococcus thermophilus* in *in vitro* system does not mean that administration of the product derived from the strain DSM 11988 would prevent or treat colorectal cancer as well as other asserted conditions as presently claimed.

Without sufficient guidance, beyond that provided, the determination of prophylactic or therapeutic amount of alkaline sphingomyelinase of bacterial origin including that is derived from the strain DSM 11988 in the currently claimed method for administration is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Vera Afremova

AU 1651

April 13, 2004

VERA AFREMOVA

PATENT EXAMINER